CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76170

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW # 1

2. ANDA # 76-170

3. NAME AND ADDRESS OF APPLICANT
Barr Laboratories, Inc.
Attention: Christine Mundkur
2 Quaker Road
P. O. Box 2900
Pomona, NY 10970-0519

4. LEGAL BASIS FOR ANDA SUBMISSION
The basis of this submission is the approved listed drug, Lithobid® Extended Release Tablets, 300 mg (NDA #18-027) manufactured by Solvay Pharmaceuticals, Inc. There are no valid patents and exclusivities (pp 03-1, 03-2).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Lithium Carbonate

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
May 11, 2001: Original Submission
July 3, 2001: Refuse to File
July 26, 2001: Amendment
July 27, 2001: Acceptable for filing

10. PHARMACOLOGICAL CATEGORY
Antimanic Agent

11. Rx or OTC
Rx

12. RELATED ANDA/DMFs

13. DOSAGE FORM
Extended Release Tablets

14. POTENCY
300 mg

15. CHEMICAL NAME AND STRUCTURE

Lithium Carbonate, Dilithium carbonate Li_2CO_3 M. W. = 73.89 g/mole.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
See review

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable; Minor

19. REVIEWER
Ijeoma N. Nnamani, Ph.D.

DATE COMPLETED
October 11, 2001

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commercial

information

Chem Review #1

NOV - 6 2001

38. Chemistry comments to be provided to the applicant

ANDA: 76-170 APPLICANT: Barr Laboratories, Inc.

DRUG PRODUCT: Lithium Carbonate Extended-Release Tablets USP, 300 mg

The following deficiencies represent Minor deficiencies:

1. Please revise and resubmit your components and composition to mg/tablet instead of mg/dose.

2. DMF is deficient and the holder has been informed.

3. Please specify the expected time limit for completion of the manufacturing of the product including packaging.

4. Indicate the time frame for holding tablets in bulk containers before packaging.

5. What are your packaging limits? Include your limits on your packaging order forms.

6. Core color is included in your compression guidelines on page 12-18 but not on page 12-74 (In-process testing). Please include core color in your in-process table on page 12-74. We note that "Guidelines" on page 12-74 is the same as compression guidelines on page 12-18. Please explain when "specifications" are used, remove all reference to guidelines, and provide in-process tests, methods, and specifications. Include revisions for any changes in methods.

7. Please acknowledge that in the case of any dispute that the USP method is the compendial method and overrules your HPLC method for the drug product assay and drug release.

8. Please include specifications in your Marketed Product Stability Protocol (p 16-14) for test parameters.

9. Please submit available updated room temperature stability data for the product.

10. According to literature sources, lithium carbonate may exist in more than one crystalline form. Please provide evidence that appropriate controls are in place and set a specification for _____ purity. In addition, assess the potential for interconversion of the _____ forms during the manufacturing process.

11. We know that there could be potential dissolution and hardness issues with Lithium Carbonate products on long-term stability. Therefore, include test and specification for hardness in your stability protocol and provide additional controlled room temperature data to support your expiration period.

Sincerely yours,

/S/

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

NOV - 6 2001

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Sincerely yours,

/S/

for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

1. CHEMISTRY REVIEW # 2

2. ANDA # 76-170

3. NAME AND ADDRESS OF APPLICANT
Barr Laboratories, Inc.
Attention: Christine Mundkur
2 Quaker Road
P. O. Box 2900
Pomona, NY 10970-0519

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9. AMENDMENTS AND OTHER DATES:
May 11, 2001: Original Submission
July 3, 2001: Refuse to File
July 26, 2001: Amendment
July 27, 2001: Acceptable for filing
November 6, 2001: CMC deficiencies
December 28, 2001: CMC response, Minor amendment
January 22, 2002: Bioequivalence amendment
February 25, May 29, 2002: Phone call by chemist for T amendment
March 4, 2002: Telephone amendment
March 13, 2002: Telephone amendment
March 28, 2002: Label amendment
April 8, 2002: Label amendment
May 29, 2002: Telephone amendment

10. PHARMACOLOGICAL CATEGORY
Antimanic Agent

11. R or OTC
R

12. RELATED ANDA/DMFs

13. DOSAGE FORM
Extended Release Tablets

14. POTENCY
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15. CHEMICAL NAME AND STRUCTURE

Lithium Carbonate, Dilithium carbonate Li_2CO_3 M. W. = 73.89 g/mole.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
NA

18. CONCLUSIONS AND RECOMMENDATIONS
No outstanding CMC issues; approval recommended.

19. REVIEWER
Radhika Rajagopalan, Ph.D.

DATE COMPLETED
April 12, 2002

/S/ 5/3/02

5/31/02

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Chem Review #2